10/540057

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NEWS 15 MAR 06 INPADOCDB and INPAFAMDB enhanced with new display formats
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NEWS 25 APR 28 CAS patent authority coverage expanded
NEWS 26 APR 28 ENCOMPLIT/ENCOMPLIT2 search fields enhanced
NEWS 27 APR 28 Limits doubled for structure searching in CAS REGISTRY
NEWS 28 MAY 08 STN Express, Version 8.4, now available
NEWS 29 MAY 11 STN on the Web enhanced
NEWS 30 MAY 11 BEILSTEIN substance information now available on STN Easy
NEWS 31 MAY 14 DGENE, PCTGEN and USGENE enhanced with increased limits for exact sequence match searches and introduction of free HIT display format

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L1      STRUCTURE UPLOADED

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L2      STRUCTURE UPLOADED

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SAMPLE SCREEN SEARCH COMPLETED -      665 TO ITERATE

100.0% PROCESSED      665 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       11753 TO    14847
PROJECTED ANSWERS:              0 TO        0

L3            0 SEA SSS SAM L1

-> s l1 full
FULL SEARCH INITIATED 12:15:59 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    13259 TO ITERATE
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SEARCH TIME: 00.00.01

L4          12 SEA SSS FUL L1

=> s l2
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SEARCH TIME: 00.00.01

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                        BATCH   **COMPLETE**
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PROJECTED ANSWERS:              0 TO        0

L5             0 SEA SSS SAM L2

=> s l2 full
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FULL SCREEN SEARCH COMPLETED -    22356 TO ITERATE

100.0% PROCESSED    22356 ITERATIONS                          1 ANSWERS
SEARCH TIME: 00.00.02

L6             1 SEA SSS FUL L2

=> d scan

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IN   Phenol, 5-[2-(4-chlorophenyl)ethoxy]-2-[6-[3-(diethylamino)propoxy]-1H-
     benzimidazol-2-yl]-, 1-methanesulfonate
MF   C29 H34 Cl N3 O5 S
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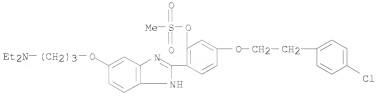

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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**


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=> d his

     (FILE 'HOME' ENTERED AT 12:13:33 ON 15 MAY 2009)

     FILE 'REGISTRY' ENTERED AT 12:13:54 ON 15 MAY 2009
L1             STRUCTURE UPLOADED
L2             STRUCTURE UPLOADED
L3           0 S L1
L4          12 S L1 FULL
L5           0 S L2
L6           1 S L2 FULL

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                             372.72     372.94

FILE 'CAPLUS' ENTERED AT 12:16:32 ON 15 MAY 2009
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FILE COVERS 1907 - 15 May 2009 VOL 150 ISS 21
FILE LAST UPDATED: 14 May 2009 (20090514/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2009

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=> s l4
L7 7 l4

=> d bib abs hitstr 1-7 17

L7 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2008:705768 CAPLUS
DN 149:47695
TI Compounds and methods for enzyme-mediated tumor imaging and therapy
IN Kassis, Amin I.
PA President and Fellows of Harvard College, USA
SO PCT Int. Appl., 116pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

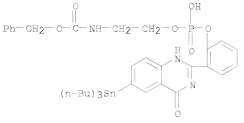
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2008069976	A2	20080612	WO 2007-US24659	20071130
	WO 2008069976	A3	20081016		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

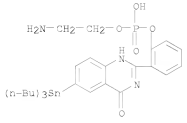
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRAI	US 2006-872073P	P	20061201
	US 2007-912688P	P	20070419
	US 2007-949240P	P	20070711

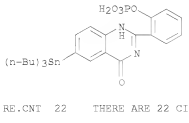
OS MARPAT 149:47695
AB The invention provides methods and compns., e.g., for tumor imaging and therapy.
IT 1032084-05-1P 1032084-08-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(enzyme-mediated tumor imaging and therapy)
RN 1032084-05-1 CAPLUS
CN Carbamic acid, N-[2-[[[2-[3,4-dihydro-4-oxo-6-(tributylstannyl)-2-quinazolinyl]phenoxy]hydroxyphosphinyl]oxy]ethyl]-, phenylmethyl ester (CA INDEX NAME)



RN 1032084-08-4 CAPLUS
CN Phosphoric acid, mono(2-aminoethyl) mono[2-[3,4-dihydro-4-oxo-6-(tributylstannyl)-2-quinazolinyl]phenyl] ester (CA INDEX NAME)



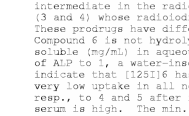
L7 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2007:1322671 CAPLUS
DN 149:402586
TI DMSO increases radioiodination yield of radiopharmaceuticals
AU Wang, Ketai; Adelstein, S. James; Kassis, Amin I.
CS Department of Radiology, Harvard Medical School, Boston, MA, 02115, USA
SO Applied Radiation and Isotopes (2007), Volume Date 2008, 66(1), 50-59
CODEN: ARISEF; ISSN: 0969-8043
PB Elsevier Ltd.
DT Journal
LA English
OS CASREACT 149:402586
AB A high-yielding radioiodination method for various types of mols. is described. The approach employs DMSO as precursor solvent, a reaction ratio of 2-5 precursor mols. per iodine atom, 5-10 μg oxidant, and a 10-25 μL reaction volume The solution is vortexed at room temperature for 1-5 min and progress of the reaction is assessed by HPLC. Radioiodinated products are obtained in ≥95% yield and meet the requirements for radiotracer imaging, biodistribution studies, and mol. and cellular biol. research.
IT 683202-94-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(DMSO-mediated radioiodination of pharmaceutical compds. and efficient synthesis of radiopharmaceuticals)
RN 683202-94-0 CAPLUS
CN 4(3H)-Quinazolinone, 2-[2-(phosphonooxy)phenyl]-6-(tributylstannyl)- (CA INDEX NAME)



RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

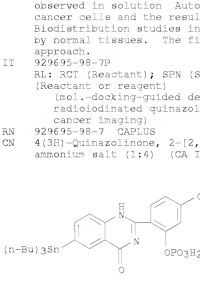
L7 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2007:342095 CAPLUS
DN 146:517116
TI Evaluation of chemical, physical, and biologic properties of tumor-targeting radioiodinated quinazolinone derivative
AU Wang, Ketai; Kirichian, Agop M.; Al Aowad, Ayman F.; Adelstein, S. James; Kassis, Amin I.
CS Department of Radiology, Harvard Medical School, Boston, MA, 02115, USA
SO Bioconjugate Chemistry (2007), 18(3), 754-764
CODEN: BCCHES; ISSN: 1043-1802
PB American Chemical Society
DT Journal
LA English
OS CASREACT 146:517116
AB Our group is developing a novel technol., enzyme-mediated cancer imaging and therapy (EMCIT), that aims to entrap radioiodinated compds. within solid tumors for noninvasive tumor detection and therapy. In this approach, a water-soluble, radioiodinated prodrug is hydrolyzed in vivo to a highly water-insol. compound by an enzyme overexpressed extracellularly by tumor cells. We have synthesized and characterized the water-soluble prodrug, 2-(2'-phosphoryloxyphenyl)-6-[125I]iodo-4-(3H)-quinazolinone [125I]5, which is readily hydrolyzed by alkaline phosphatase, an enzyme expressed by many tumor cell lines, to a water-insol. drug, 2-(2'-hydroxyphenyl)-6-[125I]iodo-4-(3H)-quinazolinone [125I]1. In the course of our study, we discovered that ammonium 2-(2'-phosphoryloxyphenyl)-6-tributylstannyl-4-(3H)-quinazolinone, an intermediate in the radioiodination of the prodrug, exists as two isomers (3 and 4) whose radioiodination leads, resp., to [125I]6 and [125I]5. These prodrugs have different in vitro and in vivo biol. activities. Compound 6 is not hydrolyzed by alkaline phosphatase (ALP), whereas 5 is highly soluble (mg/mL) in aqueous solution and is rapidly dephosphorylated in the presence of ALP to 1, a water-insol. mol. (ng/mL). Mouse biodistribution studies indicate that [125I]6 has high uptake in kidney and liver and [125I]5 has very low uptake in all normal organs. Compds. 3 and 6 are converted, resp., to 4 and 5 after incubation in DMSO. The stability of 5 in human serum is high. The min. ALP concentration needed to hydrolyze 5 is much greater than the ALP level in the blood of patients with cancer, and the latter should not affect the pharmacokinetics of the compound Incubation of 5 with viable human and mouse tumor-cell lines-but not with normal human cells and mouse tissues-leads to its hydrolysis and the formation of large crystals of 1. We expect that 5 will also be hydrolyzed in vivo by tumor cells that express phosphatase activity extracellularly and anticipate the specific precipitation of radioiodinated 1 within tumor cell clusters. This should lead to high tumor-to-normal-tissue ratios and enable imaging (SPECT/PET) and radionuclide therapy of solid tumors.
IT 414902-18-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(tumor-targeting radioiodinated quinazolinone derivative for tumor imaging and radiotherapy)
RN 414902-18-4 CAPLUS
CN 4(3H)-Quinazolinone, 2-[2-(phosphonooxy)phenyl]-6-(tributylstannyl)-, ammonium salt (1:2) (CA INDEX NAME)



● 2 NH_3

RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2007:107522 CAPLUS
DN 146:358795
TI Molecular-Docking-Guided Design, Synthesis, and Biologic Evaluation of Radioiodinated Quinazolinone Prodrugs
AU Chen, Kai; Al Aowad, Ayman F.; Adelstein, S. James; Kassis, Amin I.
CS Department of Radiology, Harvard Medical School, Boston, MA, 02115, USA
SO Journal of Medicinal Chemistry (2007), 50(4), 663-673
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 146:358795
AB Enzyme-mediated cancer imaging and therapy (EMCIT) is a novel approach in which radioactive water-soluble mols. are precipitated in vivo following their hydrolysis by extracellular enzymes overexpressed by cancer cells. AutoDock 3.0 was used to model the interaction-binding between a series of iodinated quinazolinone derivs. and human placental alkaline phosphatase (PLAP) and to assess the effects of structural modification of the derivs. Ammonium 2-(2',4'-diphosphoryloxyphenyl)-6-iodo-4-(3H)-quinazolinone (I), having the most favorable calculated inhibition constant, was synthesized and characterized. Concentration-dependent, PLAP-mediated conversion of I or its 125I-labeled isotopomer (II) to water-insol. 2-(2',4'-dihydroxyphenyl)-6-[127I/125I]iodo-4-(3H)-quinazolinones was observed in solution Autoradiog. indicated that II is hydrolyzed by human cancer cells and the resulting product ppts. on exterior cell surfaces. Biodistribution studies in mice demonstrated that II is minimally retained by normal tissues. The findings support the validity of the EMCIT approach.
IT 929695-98-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(mol.-docking-guided design, synthesis, and biol. evaluation of radioiodinated quinazolinone phosphates as prodrugs for enzyme-mediated cancer imaging)
RN 929695-98-7 CAPLUS
CN 4(3H)-Quinazolinone, 2-[2,4-bis(phosphonooxy)phenyl]-6-(tributylstannyl)-, ammonium salt (1:4) (CA INDEX NAME)



●4 NH_3

RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

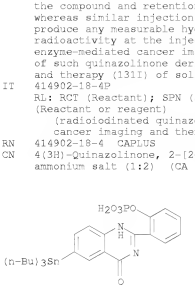
L7 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2006:1323336 CAPLUS
DN 146:290529
TI In silico design, synthesis, and biological evaluation of radioiodinated quinazolinone derivatives for alkaline phosphatase-mediated cancer diagnosis and therapy
AU Chen, Kai; Wang, Ketai; Kirichian, Agop M.; Al Aowad, Ayman F.; Iyer, Lakshmanan K.; Adelstein, S. James; Kassis, Amin I.
CS Department of Radiology, Harvard Medical School, Harvard University, Cambridge, MA, USA
SO Molecular Cancer Therapeutics (2006), 5(12), 3001-3013
CODEN: MCTOCP; ISSN: 1535-7163
PB American Association for Cancer Research
DT Journal
LA English

AB As part of the development of enzyme-mediated cancer imaging and therapy, a novel technol. to entrap water-insol. radioactive mols. within solid tumors, we show that a water-soluble, radioactive quinazolinone prodrug, ammonium 2-(2'-phosphoryloxyphenyl)-6-[125I]iodo-4-(3H)-quinazolinone (125IQ2-P), is hydrolyzed by alkaline phosphatase to a water-insol., radiolabeled drug, 2-(2'-hydroxyphenyl)-6-[125I]iodo-4-(3H)-quinazolinone (125IQ2-OH). Biodistribution data suggest the existence of two isoforms of the prodrug (IQ2-P(I) and IQ2-P), and this has been confirmed by their synthesis and characterization. Structural differences of the two isoforms have been examined using in silico mol. modeling techniques and docking methods to describe the interaction/binding between the isoforms and human placental alkaline phosphatase (PLAP), a tumor cell, membrane-associated, hydrolytic enzyme whose structure is known by X-ray crystallog. determination. Docking data show that IQ2-P, but not IQ2-P(I), fits the active binding site of PLAP favorably and interacts with the catalytic amino acid Ser92, which plays an important role in the hydrolytic process. The binding free energies (ΔGbinding) of the isoforms to PLAP predict that IQ2-P will be the better substrate for PLAP. The in vitro incubation of the isoforms with PLAP leads to the rapid hydrolysis of IQ2-P only and confirms the in silico expectations. Fluorescence microscopy shows that in vitro incubation of IQ2-P with mouse and human tumor cells causes the extracellular, alkaline phosphatase-mediated hydrolysis of the mol. and precipitation of fluorescent crystals of IQ2-OH. No hydrolysis is seen in the presence of normal mouse and human cells. Furthermore, the intratumoral injection of 125IQ2-P into alkaline phosphatase-expressing solid human tumors grown s.c. in nude rats results in efficient hydrolysis of the compound and retention of .apprx.70% of the injected radioactivity, whereas similar injection into normal tissues (e.g., muscle) does not produce any measurable hydrolysis (.apprx.1%) or retention of radioactivity at the injected site. These studies support the enzyme-mediated cancer imaging and therapy technol. and show the potential of such quinazolinone derivs. in the in vivo radio-detection (123I/124I) and therapy (131I) of solid tumors.

IT 414902-18-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(radioiodinated quinazolinone derivs. for alkaline phosphatase-mediated cancer imaging and therapy)

RN 414902-18-4 CAPLUS

CN 4(3H)-Quinazolinone, 2-[2-(phosphonooxy)phenyl]-6-(tributylstannyl)-, ammonium salt (1:2) (CA INDEX NAME)



RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2004:566630 CAPLUS
DN 141:102235
TI Membrane-permeable fluorogenic enzyme substrates and methods of preparation
IN Goeman, Jan Ludwig; Van Acker, Koenraad Lodewijk August; Van Der Eycken, Johan Theo Andre; Dierynck, Inge
PA Tibotec Bvba, Belg.
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004058787	A2	20040715	WO 2003-EP51105	20031226
	WO 2004058787	A3	20050120		
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	JP 2006514650	T	20060511	JP 2004-563251	20031226
	IN 2005DN01888	A	20070406	IN 2005-DN1888	20050505
	US 20070037234	A1	20070215	US 2006-540057	20061103
PRAI	EP 2002-102898	A	20021227		
	WO 2003-EP51105	W	20031226		

OS MARPAT 141:102235

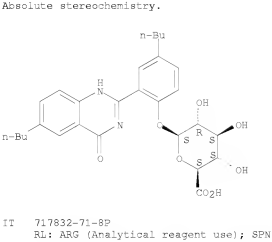
AB This invention relates to enzyme, e.g., hydrolase, fluorogenic substrates with improved cell permeability, methods for the preparation thereof, and methods of measuring activities of enzymes, particularly in cell-based assays. The substrates easily diffuse into the cells, where they are enzymically processed to yield photostable fluorescent products, and are particularly fitted for visualizing enzyme-derived activities in cell-based assays. Thus, 2-phenyl-3H-quinazoline-4-one derivs. were synthesized. One such fluorogenic substrate, 1-O-(2-(4-oxo-6-n-butyl-3H-quinazolinyl)-4-n-butylphenyl)-β-D-glucuronic acid was used to determine the effectiveness of introduction of a GUS expression plasmid into plant cells by electroporation.

IT 717832-74-1
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(membrane-permeable fluorogenic enzyme substrates and methods of preparation)

RN 717832-74-1 CAPLUS

CN β-D-Glucopyranosiduronic acid, 4-butyl-2-(6-butyl-1,4-dihydro-4-oxo-2-quinazolinyl)phenyl (9CI) (CA INDEX NAME)

Absolute stereochemistry.



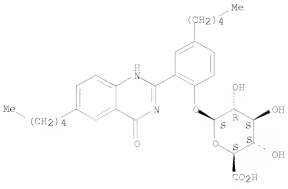
IT 717832-71-8P
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(membrane-permeable fluorogenic enzyme substrates and methods of preparation)

RN 717832-71-8 CAPLUS

CN β-D-Glucopyranosiduronic acid, 2-(1,4-dihydro-4-oxo-6-pentyl-2-quinazolinyl)-4-pentylphenyl (9CI) (CA

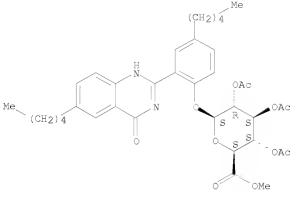
INDEX NAME)

Absolute stereochemistry.



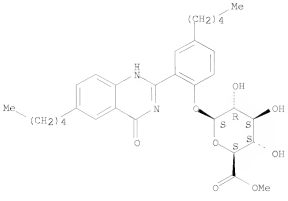
IT 717832-69-4P 717832-70-7P 717832-72-9P
717832-73-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(membrane-permeable fluorogenic enzyme substrates and methods of preparation)
RN 717832-69-4 CAPLUS
CN β-D-Glucopyranosiduronic acid,
2-(1,4-dihydro-4-oxo-6-pentyl-2-quinazolinyl)-4-pentylphenyl, methyl ester, 2,3,4-triacetate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

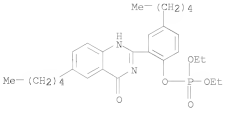


RN 717832-70-7 CAPLUS
CN β-D-Glucopyranosiduronic acid,
2-(1,4-dihydro-4-oxo-6-pentyl-2-quinazolinyl)-4-pentylphenyl, methyl ester (9CI) (CA INDEX NAME)

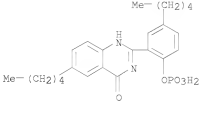
Absolute stereochemistry.



RN 717832-72-9 CAPLUS
CN Phosphoric acid, 2-(1,4-dihydro-4-oxo-6-pentyl-2-quinazolinyl)-4-pentylphenyl diethyl ester (9CI) (CA INDEX NAME)



RN 717832-73-0 CAPLUS
CN 4(3H)-Quinazolinone, 6-pentyl-2-[5-pentyl-2-(phosphonooxy)phenyl]- (CA INDEX NAME)



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

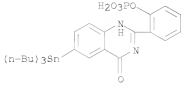
L7 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2002:149217 CAPLUS
DN 136:321360
TI Synthesis and Biologic Evaluation of a Radioiodinated Quinazolinone Derivative for Enzyme-Mediated Insolubilization Therapy
AU Ho, Nanhui; Harapanhalli, Ravi S.; Dahman, Bassam A.; Chen, Kai; Wang, Ketai; Adelstein, S. James; Kassis, Amin I.
CS Department of Radiology, Harvard Medical School, Boston, MA, 02115, USA
SO Bioconjugate Chemistry (2002), 13(2), 357-364
CODEN: BCCHES; ISSN: 1043-1802
PB American Chemical Society
DT Journal
LA English
AB We have developed a new strategy that aims to concentrate therapeutic radionuclides within solid tumors. This approach, which we have named EMIT (enzyme-mediated insolubilization therapy), is a method for enzyme-dependent, site-specific, in vivo precipitation of a radioactive mol. (from a water-soluble precursor) within the extracellular space of solid tumors.

The prodrug, ammonium 2-(2'-phosphoryloxyphenyl)-6-iodo-4-(3H)-quinazolinone, labeled with iodine-125 (125IPD) and its authentic compound labeled with iodine-127 (IPD) have been synthesized, purified, and characterized. The alkaline phosphatase (ALP)-mediated conversion of these water-soluble nonfluorescent prodrugs to the water-insol. fluorescent species, iodine-123-labeled 2-(2'-hydroxyphenyl)-6-iodo-4-(3H)-quinazolinone (123ID) and its iodine-127-labeled derivative (ID), has been demonstrated in vitro. Biodistribution studies in mice indicate that both 125IPD and 125ID are minimally retained by most tissues and organs. In addition, following its i.v. injection in mice, 125IPD is localized in ALP-rich regions and converted to 125ID, which remains indefinitely within the tissues where it is produced. We believe that EMIT is a strategy that will lead to the active and specific concentration and entrapment of therapeutic radionuclides within solid tumors, the consequent protracted irradiation of tumor cells within the range of the emitted particles, and the effective therapy of solid tumors.

IT 414902-18-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and biol. evaluation of radioiodinated quinazolinone derivative for enzyme-mediated insolubilization therapy)

RN 414902-18-4 CAPLUS

CN 4(3H)-Quinazolinone, 2-[2-(phosphonooxy)phenyl]-6-(tributylstannyl)-, ammonium salt (1:2) (CA INDEX NAME)



●2 NH_3

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	44.98	417.92
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-5.74	-5.74

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L8      STRUCTURE UPLOADED

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L9      STRUCTURE UPLOADED

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SAMPLE SCREEN SEARCH COMPLETED -      263 TO ITERATE

100.0% PROCESSED      263 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:         4287 TO     6233
PROJECTED ANSWERS:               0 TO        0

L13           0 SEA SSS SAM L8

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FULL SEARCH INITIATED 12:25:15 FILE 'REGISTRY'
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SEARCH TIME: 00.00.01

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SEARCH TIME: 00.00.02

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-> s l10 full
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FULL SCREEN SEARCH COMPLETED -     3632 TO ITERATE

100.0% PROCESSED     3632 ITERATIONS                                1 ANSWERS
SEARCH TIME: 00.00.01

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-> s l12 full
FULL SEARCH INITIATED 12:25:36 FILE 'REGISTRY'
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10/540057

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SEARCH TIME: 00.00.01

L17 6 SEA SSS FUL L12

-> d his

(FILE 'HOME' ENTERED AT 12:13:33 ON 15 MAY 2009)

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L2 STRUCTURE UPLOADED
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L4 12 S L1 FULL
L5 0 S L2
L6 1 S L2 FULL

FILE 'CAPLUS' ENTERED AT 12:16:32 ON 15 MAY 2009
L7 7 S L4

FILE 'REGISTRY' ENTERED AT 12:22:55 ON 15 MAY 2009
L8 STRUCTURE UPLOADED
L9 STRUCTURE UPLOADED
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L15 1 S L9 FULL
L16 1 S L10 FULL
L17 6 S L12 FULL

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COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
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FILE COVERS 1907 - 15 May 2009 VOL 150 ISS 21
FILE LAST UPDATED: 14 May 2009 (20090514/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2009

CAplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2008.

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This file contains CAS Registry Numbers for easy and accurate

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MISSING OPERATOR L4 L6
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l4 or l6 or l15 or l16 or l17
             7 L4
             1 L6
             1 L15
             1 L16
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L18          9 L4 OR L6 OR L15 OR L16 OR L17

=> d bib abs hitstr 1-9 l18

L18  ANSWER 1 OF 9  CAPLUS  COPYRIGHT 2009 ACS on STN
AN   2008:1085748  CAPLUS
DN   149:438757
TI   A Novel Deep Blue-Emitting ZnII Complex Based on Carbazole-Modified
     2-(2-Hydroxyphenyl)benzimidazole: Synthesis, Bright Electroluminescence,
     and Substitution Effect on Photoluminescent, Thermal, and Electrochemical
     Properties
AU   Xu, Hui; Xu, Zhi-Feng; Yue, Zheng-Yu; Yan, Peng-Fei; Wang, Bin; Jia,
     Li-Wei; Li, Guang-Ming; Sun, Wen-Bin; Zhang, Ju-Wen
CS   School of Chemistry and Materials, Heilongjiang University, Harbin,
     150080, Peop. Rep. China
SO   Journal of Physical Chemistry C (2008), 112(39), 15517-15525
     CODEN: JPCCCK; ISSN: 1932-7447
PB   American Chemical Society
DT   Journal
LA   English
OS   CASREACT 149:438757
AB   A novel deep blue-emitting ZnII complex, Zn(Lc)2 (Lc- =
     2-(1-[6-(9H-carbazol-9-yl)hexyl]-1H-benzo[d]imidazol-2-yl)phenolate) based
     on a carbazole-functionalized N,cxa.O ligand was synthesized by a modified
     method.  Other two ZnII complexes (Zn(La)2, La- =
     2-(1H-benzo[d]imidazol-2-yl)phenolate; Zn(Lb)2, Lb- =
     2-(1-ethyl-1H-benzo[d]imidazol-2-yl)phenolate) were also prepared for
     comparison.  The remarkable substitution effect on the photoluminescent
     and thermal properties of the complexes was studied.  The study indicated
     an unexpected amplifying hypsochromic effect of the substituents on the
     emission of the complex in the solid state: the larger substituent
     corresponded to the larger blue shift of the emission of Zn(Lc)2 has the
     shortest emission wavelength of 422 nm as the deep blue emission among
     these three complexes.  The stronger steric effect induced by the bulky
     substitutions should be one of the most important factors.  Among the
     three ZnII complexes, the temperature of decomposition of Zn(Lc)2 is the highest at
     427°.  Cyclic voltammetry (CV) of the complexes showed that the
     carbazole moieties remarkably improved the hole injection ability of
     Zn(Lc)2 with the HOMO energy level 0.6 eV higher than those of Zn(La)2 and
     Zn(Lb)2.  The good hole injection and transporting ability of Zn(Lc)2 was
     further proved by its three-layer devices, in which the electroluminescent
     (EL) emission mainly originated from the electron-transporting Alq3 layer.
     Through the four-layer devices with the hole-blocking layer, the pure blue
     emission of Zn(Lc)2 at 452 nm was demonstrated. Zn(Lc)2 seems favorable
     among the blue-emitting ZnII complexes with a brightness >2000 cd m-2, a
     high efficiency stability, and an excellent EL spectra stability.
IT   1065005-98-2P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation of N-modified (hydroxyphenyl)benzimidazoles, their zinc(II)
        complexes, and luminescence, thermal and electroluminescence
        properties)
RN   1065005-98-2  CAPLUS
CN   Phenol, 2-[1-[6-(9H-carbazol-9-yl)hexyl]-1H-benzimidazol-2-yl]-,
     1-(4-methylbenzenesulfonate)  (CA INDEX NAME)
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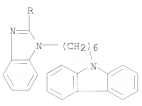
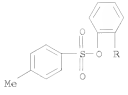


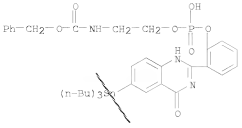


RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

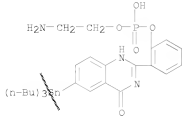
L18 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2008:705768 CAPLUS
DN 149:476795
TI Compounds and methods for enzyme-mediated tumor imaging and therapy
IN Kassis, Amin I.
PA President and Fellows of Harvard College, USA
SO PCT Int. Appl., 116pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2008069976	A2	20080612	WO 2007-US24659	20071130
	WO 2008069976	A3	20081016		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW		
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA		
PRAI	US 2006-872073P	P	20061201		
	US 2007-912688P	P	20070419		
	US 2007-949240P	P	20070711		

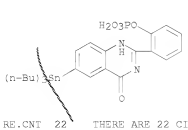
OS MARPAT 149:476795
AB The invention provides methods and compns., e.g., for tumor imaging and therapy.
IT 1032084-05-1P 1032084-08-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(enzyme-mediated tumor imaging and therapy)
RN 1032084-05-1 CAPLUS
CN Carbamic acid, N-[2-[[[2-[3,4-dihydro-4-oxo-6-(tributylstannyl)-2-quinazolinyl]phenoxy]hydroxyphosphinyl]oxy]ethyl]-, phenylmethyl ester (CA INDEX NAME)



RN 1032084-08-4 CAPLUS
CN Phosphoric acid, mono(2-aminoethyl)
mono[2-[3,4-dihydro-4-oxo-6-(tributylstannyl)-2-quinazolinyl]phenyl] ester
(CA INDEX NAME)

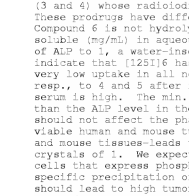


L18 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2007:1322671 CAPLUS
DN 149:402586
TI DMSO increases radioiodination yield of radiopharmaceuticals
AU Wang, Ketai; Adelstein, S. James; Kassis, Amin I.
CS Department of Radiology, Harvard Medical School, Boston, MA, 02115, USA
SO Applied Radiation and Isotopes (2007), Volume Date 2008, 66(1), 50-59
CODEN: ARISEF; ISSN: 0969-8043
PB Elsevier Ltd.
DT Journal
LA English
OS CASREACT 149:402586
AB A high-yielding radioiodination method for various types of mols. is described. The approach employs DMSO as precursor solvent, a reaction ratio of 2-5 precursor mols. per iodine atom, 5-10 μg oxidant, and a 10-25 μl reaction volume The solution is vortexed at room temperature for 1-5 min and progress of the reaction is assessed by HPLC. Radioiodinated products are obtained in ≥95% yield and meet the requirements for radiotracer imaging, biodistribution studies, and mol. and cellular biol. research.
IT 683202-94-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(DMSO-mediated radioiodination of pharmaceutical compds. and efficient synthesis of radiopharmaceuticals)
RN 683202-94-0 CAPLUS
CN 4(3H)-Quinazolinone, 2-[2-(phosphonooxy)phenyl]-6-(tributylstannyl)- (CA INDEX NAME)



RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2007:342095 CAPLUS
DN 146:517116
TI Evaluation of chemical, physical, and biologic properties of tumor-targeting radioiodinated quinazolinone derivative
AU Wang, Ketai; Kirichian, Agop M.; Al Aowad, Ayman F.; Adelstein, S. James; Kassis, Amin I.
CS Department of Radiology, Harvard Medical School, Boston, MA, 02115, USA
SO Bioconjugate Chemistry (2007), 18(3), 754-764
CODEN: BCCHES; ISSN: 1043-1802
PB American Chemical Society
DT Journal
LA English
OS CASREACT 146:517116
AB Our group is developing a novel technol., enzyme-mediated cancer imaging and therapy (EMCIT), that aims to entrap radioiodinated compds. within solid tumors for noninvasive tumor detection and therapy. In this approach, a water-soluble, radioiodinated prodrug is hydrolyzed in vivo to a highly water-insol. compound by an enzyme overexpressed extracellularly by tumor cells. We have synthesized and characterized the water-soluble prodrug, 2-(2'-phosphoryloxyphenyl)-6-[125I]iodo-4-(3H)-quinazolinone [125I]5, which is readily hydrolyzed by alkaline phosphatase, an enzyme expressed by many tumor cell lines, to a water-insol. drug, 2-(2'-hydroxyphenyl)-6-[125I]iodo-4-(3H)-quinazolinone [125I]1. In the course of our study, we discovered that ammonium 2-(2'-phosphoryloxyphenyl)-6-tributylstannyl-4-(3H)-quinazolinone, an intermediate in the radioiodination of the prodrug, exists as two isomers (3 and 4) whose radioiodination leads, resp., to [125I]6 and [125I]5. These prodrugs have different in vitro and in vivo biol. activities. Compound 6 is not hydrolyzed by alkaline phosphatase (ALP), whereas 5 is highly soluble (mg/mL) in aqueous solution and is rapidly dephosphorylated in the presence of ALP to 1, a water-insol. mol. (ng/mL). Mouse biodistribution studies indicate that [125I]6 has high uptake in kidney and liver and [125I]5 has very low uptake in all normal organs. Compds. 3 and 6 are converted, resp., to 4 and 5 after incubation in DMSO. The stability of 5 in human serum is high. The min. ALP concentration needed to hydrolyze 5 is much greater than the ALP level in the blood of patients with cancer, and the latter should not affect the pharmacokinetics of the compound. Incubation of 5 with viable human and mouse tumor-cell lines-but not with normal human cells and mouse tissues-leads to its hydrolysis and the formation of large crystals of 1. We expect that 5 will also be hydrolyzed in vivo by tumor cells that express phosphatase activity extracellularly and anticipate the specific precipitation of radioiodinated 1 within tumor cell clusters. This should lead to high tumor-to-normal-tissue ratios and enable imaging (SPECT/PET) and radionuclide therapy of solid tumors.
IT 414902-18-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(tumor-targeting radioiodinated quinazolinone derivative for tumor imaging and radiotherapy)
RN 414902-18-4 CAPLUS
CN 4(3H)-Quinazolinone, 2-[2-(phosphonooxy)phenyl]-6-(tributylstannyl)-, ammonium salt (1:2) (CA INDEX NAME)

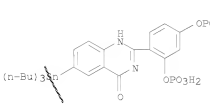


●2 NH_3

RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2007:107522 CAPLUS
DN 146:358795
TI Molecular-Docking-Guided Design, Synthesis, and Biologic Evaluation of Radioiodinated Quinazolinone Prodrugs
AU Chen, Kai; Al Aowad, Ayman F.; Adelstein, S. James; Kassis, Amin I.
CS Department of Radiology, Harvard Medical School, Boston, MA, 02115, USA
SO Journal of Medicinal Chemistry (2007), 50(4), 663-673
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 146:358795
AB Enzyme-mediated cancer imaging and therapy (EMCIT) is a novel approach in which radioactive water-soluble mols. are precipitated in vivo following their hydrolysis by extracellular enzymes overexpressed by cancer cells. AutoDock 3.0 was used to model the interaction-binding between a series of iodinated quinazolinone derivs. and human placental alkaline phosphatase (PLAP) and to assess the effects of structural modification of the derivs. Ammonium 2-(2',4'-diphosphoryloxyphenyl)-6-iodo-4-(3H)-quinazolinone (I), having the most favorable calculated inhibition constant, was synthesized and characterized. Concentration-dependent, PLAP-mediated conversion of I or its 125I-labeled isotopomer (II) to water-insol. 2-(2',4'-dihydroxyphenyl)-6-[127I/125I]iodo-4-(3H)-quinazolinones was observed in solution Autoradiog. indicated that II is hydrolyzed by human cancer cells and the resulting product ppts. on exterior cell surfaces. Biodistribution studies in mice demonstrated that II is minimally retained by normal tissues. The findings support the validity of the EMCIT approach.
IT 929695-98-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(mol.-docking-guided design, synthesis, and biol. evaluation of radioiodinated quinazolinone phosphates as prodrugs for enzyme-mediated cancer imaging)
RN 929695-98-7 CAPLUS
CN 4(3H)-Quinazolinone, 2-[2,4-bis(phosphonooxy)phenyl]-6-(tributylstannyl)-, ammonium salt (1:4) (CA INDEX NAME)



●4 NH3

RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

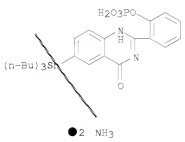
L18 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2006:1323336 CAPLUS
DN 146:290529
TI In silico design, synthesis, and biological evaluation of radioiodinated quinazolinone derivatives for alkaline phosphatase-mediated cancer diagnosis and therapy
AU Chen, Kai; Wang, Ketai; Kirichian, Agop M.; Al Aowad, Ayman F.; Iyer, Lakshmanan K.; Adelstein, S. James; Kassis, Amin I.
CS Department of Radiology, Harvard Medical School, Harvard University, Cambridge, MA, USA
SO Molecular Cancer Therapeutics (2006), 5(12), 3001-3013
CODEN: MCTOCF; ISSN: 1535-7163
PB American Association for Cancer Research
DT Journal
LA English
AB As part of the development of enzyme-mediated cancer imaging and therapy, a novel technol. to entrap water-insol. radioactive mols. within solid

tumors, we show that a water-soluble, radioactive quinazolinone prodrug, ammonium 2-(2'-phosphoryloxyphenyl)-6-[125I]iodo-4-(3H)-quinazolinone (125IQ2-P), is hydrolyzed by alkaline phosphatase to a water-insol., radiolabeled drug, 2-(2'-hydroxyphenyl)-6-[125I]iodo-4-(3H)-quinazolinone (125IQ2-OH). Biodistribution data suggest the existence of two isoforms of the prodrug (IQ2-P(I) and IQ2-P), and this has been confirmed by their synthesis and characterization. Structural differences of the two isoforms have been examined using in silico mol. modeling techniques and docking methods to describe the interaction/binding between the isoforms and human placental alkaline phosphatase (PLAP), a tumor cell, membrane-associated, hydrolytic enzyme whose structure is known by X-ray crystallog. determination. Docking data show that IQ2-P, but not IQ2-P(I), fits the active binding site of PLAP favorably and interacts with the catalytic amino acid Ser92, which plays an important role in the hydrolytic process. The binding free energies (ΔGbinding) of the isoforms to PLAP predict that IQ2-P will be the better substrate for PLAP. The in vitro incubation of the isoforms with PLAP leads to the rapid hydrolysis of IQ2-P only and confirms the in silico expectations. Fluorescence microscopy shows that in vitro incubation of IQ2-P with mouse and human tumor cells causes the extracellular, alkaline phosphatase-mediated hydrolysis of the mol. and precipitation of fluorescent crystals of IQ2-OH. No hydrolysis is seen in the presence of normal mouse and human cells. Furthermore, the intratumoral injection of 125IQ2-P into alkaline phosphatase-expressing solid human tumors grown s.c. in nude rats results in efficient hydrolysis of the compound and retention of .apprx.70% of the injected radioactivity, whereas similar injection into normal tissues (e.g., muscle) does not produce any measurable hydrolysis (.apprx.1%) or retention of radioactivity at the injected site. These studies support the enzyme-mediated cancer imaging and therapy technol. and show the potential of such quinazolinone derivs. in the in vivo radio-detection (123I/124I) and therapy (131I) of solid tumors.

IT 414902-18-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(radioiodinated quinazolinone derivs. for alkaline phosphatase-mediated cancer imaging and therapy)

RN 414902-18-4 CAPLUS

CN 4(3H)-Quinazolinone, 2-[2-(phosphonooxy)phenyl]-6-(tributylstannyl)-, ammonium salt (1:2) (CA INDEX NAME)



RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2004:566630 CAPLUS

DN 141:102235

TI Membrane-permeable fluorogenic enzyme substrates and methods of preparation

IN Goeman, Jan Ludwig; Van Acker, Koenraad Lodewijk August; Van Der Eycken, Johan Theo Andre; Dierynck, Inge

PA Tibotec Bvba, Belg.

SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2004058787 A2 20040715 WO 2003-EP51105 20031226
WO 2004058787 A3 20050120
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
CA 2506897 A1 20040715 CA 2003-2506897 20031226
AU 2003303460 A1 20040722 AU 2003-303460 20031226
EP 1578757 A2 20050928 EP 2003-808319 20031226
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
CN 1732180 A 20060208 CN 2003-80107671 20031226
JP 2006514650 T 20060511 JP 2004-563251 20031226
IN 2005DN01888 A 20070406 IN 2005-DN1888 20050505
US 20070037234 A1 20070215 US 2006-540057 20061103
PRAI EP 2002-102898 A 20021227
WO 2003-EP51105 W 20031226

OS MARPAT 141:102235

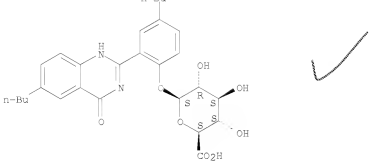
AB This invention relates to enzyme, e.g., hydrolase, fluorogenic substrates with improved cell permeability, methods for the preparation thereof, and methods of measuring activities of enzymes, particularly in cell-based assays. The substrates easily diffuse into the cells, where they are enzymically processed to yield photostable fluorescent products, and are particularly fitted for visualizing enzyme-derived activities in cell-based assays. Thus, 2-phenyl-3H-quinazoline-4-one derivs. were synthesized. One such fluorogenic substrate, 1-O-(2-(4-oxo-6-n-butyl-3H-quinazolinyl)-4-n-butylphenyl)-β-D-glucuronic acid was used to determine the effectiveness of introduction of a GUS expression plasmid into plant cells by electroporation.

IT 717832-74-1
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(membrane-permeable fluorogenic enzyme substrates and methods of preparation)

RN 717832-74-1 CAPLUS

CN β-D-Glucopyranosiduronic acid, 4-butyl-2-(6-butyl-1,4-dihydro-4-oxo-2-quinazolinyl)phenyl (9CI) (CA INDEX NAME)

Absolute stereochemistry.

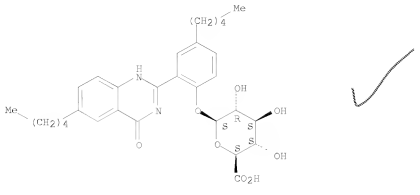


IT 717832-71-8P
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(membrane-permeable fluorogenic enzyme substrates and methods of preparation)

RN 717832-71-8 CAPLUS

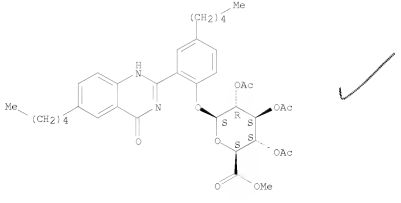
CN β-D-Glucopyranosiduronic acid, 2-(1,4-dihydro-4-oxo-6-pentyl-2-quinazolinyl)-4-pentylphenyl (9CI) (CA INDEX NAME)

Absolute stereochemistry.



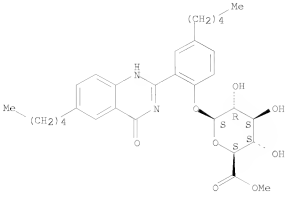
IT 717832-69-4P 717832-70-7P 717832-72-9P
717832-73-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(membrane-permeable fluorogenic enzyme substrates and methods of preparation)
RN 717832-69-4 CAPLUS
CN β-D-Glucopyranosiduronic acid,
2-(1,4-dihydro-4-oxo-6-pentyl-2-quinazolinyl)-4-pentylphenyl, methyl ester, 2,3,4-triacetate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

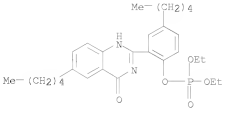


RN 717832-70-7 CAPLUS
CN β-D-Glucopyranosiduronic acid,
2-(1,4-dihydro-4-oxo-6-pentyl-2-quinazolinyl)-4-pentylphenyl, methyl ester (9CI) (CA INDEX NAME)

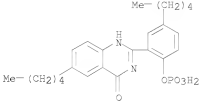
Absolute stereochemistry.



RN 717832-72-9 CAPLUS
CN Phosphoric acid, 2-(1,4-dihydro-4-oxo-6-pentyl-2-quinazolinyl)-4-pentylphenyl diethyl ester (9CI) (CA INDEX NAME)



RN 717832-73-0 CAPLUS
CN 4(3H)-Quinazolinone, 6-pentyl-2-[5-pentyl-2-(phosphonooxy)phenyl]- (CA INDEX NAME)



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2003:737580 CAPLUS
DN 139:261298
TI Preparation of imidazole and benzimidazole derivatives that inhibit the interaction of ligands with RAGE
IN Mjalli, Adnan M. M.; Andrews, Robert C.; Gopalaswamy, Ramesh; Hari, Anitha; Avor, Kwasi; Qabaja, Ghassan; Guo, Xiao-Chuan; Gupta, Suparna; Jones, David R.; Chen, Xin
PA Transtech Pharma, Inc., USA
SO PCT Int. Appl., 462 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003075921	A2	20030918	WO 2003-US6749	20030305
	WO 2003075921	A3	20031204		

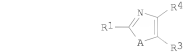
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2476594	A1	20030918	CA 2003-2476594		20030305
AU 2003217943	A1	20030922	AU 2003-217943		20030305
EP 1482931	A2	20041208	EP 2003-713918		20030305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, IR, BG, CZ, EE, HU, SK					
CN 1633290	A	20050629	CN 2003-805204		20030305
JP 2005523378	T	20050825	JP 2003-574195		20030305
AU 2007202350	A1	20070614	AU 2007-202350		20070524
AU 2007203289	A1	20070802	AU 2007-203289		20070717
JP 2009096806	A	20090507	JP 2008-271566		20081022
PRAI US 2002-361983P	P	20020305			
AU 2002-245591	A3	20020305			
AU 2003-217943	A3	20030305			
JP 2003-574195	A3	20030305			
WO 2003-US6749	W	20030305			

OS MARPAT 139:261298

GI



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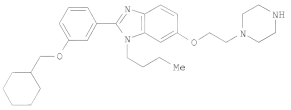
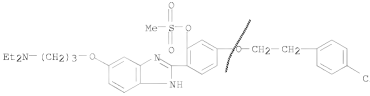


II

AB Title compds. and analogs I [wherein A = O, S, or NR2; R1 and R2 = independently H or (un)substituted (hetero)aryl, (cyclo)alkyl, heterocyclyl, alkenyl, alkynyl, alkylene(hetero)aryl, alkylene heterocyclyl, alkylene cycloalkyl, etc.; R3 and R4 = independently H, halo, OH, CN, CONH2, CO2H, or (un)substituted (hetero)aryl, (cyclo)alkyl, heterocyclyl, alkenyl, alkynyl, alkylene(hetero)aryl, alkylene heterocyclyl, alkylene cycloalkyl, etc.; and pharmaceutically acceptable salts thereof] were prepared as modulators of the interaction between the receptor for advanced glycated end products (RAGE) and its ligands, such as advanced glycated end products (AGEs), S100/calgranulin/EN-RAGE, β-amyloid, and amphoterin. For example, 1-BOC-4-[2-(4-amino-3-butylaminophenoxy)ethyl]piperazine was condensed with 3-hydroxybenzaldehyde to give the hydroxybenzimidazole. Coupling with cyclohexylmethyl bromide in the presence of NaH in THF afforded II. In binding studies employing S100b as the RAGE ligand, five hundred fifty-one invention compds. exhibited binding with IC50 values of < 10 μM. Thus, I and their pharmaceutical compns. are useful for the management, treatment, control, or as an adjunct treatment for diseases in humans caused by RAGE, including acute and chronic inflammation, the development of diabetic late complications such as increased vascular permeability, nephropathy, atherosclerosis, and retinopathy, the development of Alzheimer's disease, erectile dysfunction, and tumor invasion and metastasis (no data).

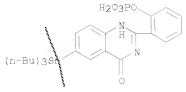
IT 603147-53-1P, Methanesulfonic acid 5-[2-(4-chlorophenyl)ethoxy]-2-[6-(3-diethylaminopropoxy)-1H-benzimidazol-

2-yl]phenyl ester
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(RAGE modulator; preparation of imidazole and benzimidazole RAGE modulators for treatment of inflammation, diabetes, tumors, and other conditions)
RN 603147-53-1 CAPLUS
CN Phenol, 5-[2-(4-chlorophenyl)ethoxy]-2-[6-[3-(diethylamino)propoxy]-1H-benzimidazol-2-yl]-, 1-methanesulfonate (CA INDEX NAME)



RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2002:149217 CAPLUS
DN 136:321360
TI Synthesis and Biologic Evaluation of a Radioiodinated Quinazolinone Derivative for Enzyme-Mediated Insolubilization Therapy
AU Ho, Nanhui; Harapanhalli, Ravi S.; Dahman, Bassam A.; Chen, Kai; Wang, Ketai; Adelstein, S. James; Kassis, Amin I.
CS Department of Radiology, Harvard Medical School, Boston, MA, 02115, USA
SO Bioconjugate Chemistry (2002), 13(2), 357-364
CODEN: BCCHES; ISSN: 1043-1802
PB American Chemical Society
DT Journal
LA English
AB We have developed a new strategy that aims to concentrate therapeutic radionuclides within solid tumors. This approach, which we have named EMIT (enzyme-mediated insolubilization therapy), is a method for enzyme-dependent, site-specific, in vivo precipitation of a radioactive mol. (from a water-soluble precursor) within the extracellular space of solid tumors. The prodrug, ammonium 2-(2'-phosphoryloxyphenyl)-6-iodo-4-(3H)-quinazolinone, labeled with iodine-125 (125IPD) and its authentic compound labeled with iodine-127 (IPD) have been synthesized, purified, and characterized. The alkaline phosphatase (ALP)-mediated conversion of these water-soluble nonfluorescent prodrugs to the water-insol. fluorescent species, iodine-125-labeled 2-(2'-hydroxyphenyl)-6-iodo-4-(3H)-quinazolinone (125ID) and its iodine-127-labeled derivative (ID), has been demonstrated in vitro. Biodistribution studies in mice indicate that both 125IPD and 125ID are minimally retained by most tissues and organs. In addition, following its i.v. injection in mice, 125IPD is localized in ALP-rich regions and converted to 125ID, which remains indefinitely within the tissues where it is produced. We believe that EMIT is a strategy that will lead to the active and specific concentration and entrapment of therapeutic radionuclides within solid tumors, the consequent protracted irradiation of tumor cells within the range of the emitted particles, and the effective therapy of solid tumors.
IT 414902-18-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and biol. evaluation of radioiodinated quinazolinone derivative for enzyme-mediated insolubilization therapy)
RN 414902-18-4 CAPLUS
CN 4(3H)-Quinazolinone, 2-[2-(phosphonooxy)phenyl]-6-(tributylstannyl)-, ammonium salt (1:2) (CA INDEX NAME)



● 2 NH_3

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT